

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference APB/PB60771	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. PCT/EP2005/003038	International filing date ( <i>day/month/year</i> ) 15 March 2005 (15.03.2005)	Priority date ( <i>day/month/year</i> ) 16 March 2004 (16.03.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant GLAXO GROUP LIMITED			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
  2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 19 September 2006 (19.09.2006)</p> <p>Authorized officer  <b>Agnes Wittmann-Regis</b></p> <p>e-mail: pt06@wipo.int</p>
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 02 AUG 2005

PCT  
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To:

see form PCT/ISA/220

29/9

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2005/003038

International filing date (day/month/year)  
15.03.2005

Priority date (day/month/year)  
16.03.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D487/04, A61K31/437, A61P29/00

Applicant  
GLAXO GROUP LIMITED

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003038

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003038

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 22-25

because:

- ☒ the said international application, or the said claims Nos. 22-25 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
  - the written form ☐ has not been furnished
  - ☐ does not comply with the standard
  - the computer readable form ☐ has not been furnished
  - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003038

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-34
	No: Claims	
Inventive step (IS)	Yes: Claims	1-34
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-21,26-34
	No: Claims	

2. Citations and explanations

see separate sheet

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

- 1) The present application relates to a pyrrolo-pyridines carrying a 1-aminocarbonyl-piperin-4-yl group in position 4, a 3,4-dimethylphenylmethyl group in position 5 and an ethyl group in position 1. The compound should be useful as PDE4-inhibitors (see test results p.44).
- 2) Cited documents  
D1: J. MED. CHEM., 16(12), 1973, pages 1340-1346  
D2: US-A-3 925 388  
D3: JP 2002 020386 A  
D4: WO 2004/024728 A  
D5: WO 2004/056823 A

Documents D4 and D5 were published after the presently claimed priority; on the presumption that the priority is valid, these documents are not considered as prior art.

- 3) Novelty  
Document D1 describes PDE inhibiting activity of a compound (37) which differs in the 4-substitution (butylamine) from the presently defined compound.  
Document D2 describes antiinflammatory, c-AMP increasing agents which differ in the 5-substitution (esters) as well as the 4-substitution (not specifically as presently defined) from that of the present application.  
D3 describes PDE4-inhibitors lacking the substitution to the 5-aminocarbonyl and with different substitutions to the 4-amino-group.

It is observed that D4 and D5 do not specifically describe the 1-aminocarbonyl-piperin-4-yl in position 4.

- 4) Inventive step  
Document D3 may be considered as closest prior art, in view of which the problem to be solved may be seen in the provision of alternative PDE4 inhibitors.  
As solution the modifications to both the groups in position 4 and 5 would not seem obvious to the person skilled in the art as the modifications are substantial whereas the prior art provides no suggestion that activity should be maintained upon such modification.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/003038

5) Further observations

Claims 22-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).